Electrophysiology Biomarkers to Aid in Diagnosis:

ERP and EEG Memory Loss Biomarkers

The Memory Loss Conundrum. Upwards of 20% of those aged 65 years and older already have detectable symptoms of mild cognitive impairment. Yet diagnosing the cause of memory loss can prove challenging. Historically, most providers have relied on self-report questionnaires and effort-based computerized testing for determining a diagnosis. Yet even when applied optimally, these assessments often fall short in the detection of early or less severe disease presentations[1,2]. Additionally, current tools often lack the sensitivity and objectivity needed to develop accurate diagnoses, resulting in a segment of the patient population that is misdiagnosed[3] and under-diagnosed[4]. Thus, when patients present with concerns of memory loss, the physician needs a very fast, easy-to-use, low-cost, objective, and sensitive test.

Electroencephalography (EEG) has been employed extensively in clinical research and provides a non-invasive and office-based solution for objectively measuring brain function. Leading research agrees that clinical evaluation along with other supportive diagnostic techniques such as functional neuroimaging may be necessary to substantiate memory loss diagnoses[5] (Figure 1). But, due to expensive and sensitive equipment along with difficult and time consuming data interpretation, EEG has historically been out of reach from practicing physicians.

eVox®: Office-Based Solution. Evoke Neuroscience, Inc. is the leading medical device company providing low cost brain electrophysiology equipment designed specifically to suit the needs of medical doctors and their patients. The eVox® system is an FDA 510(k) cleared medical device that assesses brain function to aid in diagnosis. It collects 19-channel EEG and event-related potentials (ERP) data via a portable and automated 24-channel amplifier to offer objective, brain-based biomarkers that aid in diagnosis of cognitive disorders. The physician may utilize these biomarkers to recognize early dementia conditions, identify the root cause of memory loss, and perform a differential diagnosis.

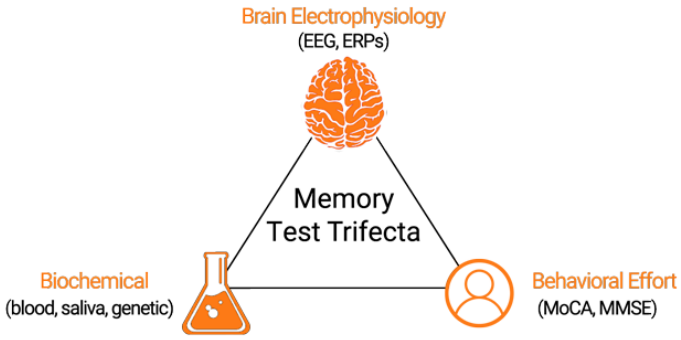

Figure 1. The highest standard of care for patients with memory loss includes assessments of brain electrophysiology, biochemical labs, and effort-based screeners.

Brain Mapping Biomarkers. Normal and productive brain function relies heavily on a complex array of interconnected networks that facilitate communication within and across brain structures. With regard to detecting and diagnosing memory loss, three electrophysiology biomarkers are particularly pertinent: 1) the P300 component of event-related potentials, 2) thalamic-generated peak alpha frequency (posterior dominant rhythm), and 3) quantitative EEG brain function scoring against a normal reference group. These biomarkers are fast and easy to obtain with the eVox® System, which utilizes cost effective equipment to facilitate an in-office assessment with limited staff training and time.

Event-Related Potentials. Memory functions and cognitive processes within the brain can be measured using event-related potentials (ERPs)[6]. These waveforms represent time-locked neuronal responses generated in response to specific events or stimuli. The time delay, or latency, between stimulus onset and a patient's physical response reflects brain processing speed, while waveform amplitude reflects neuronal recruitment and subsequent activation (i.e., how many neurons are successfully working together to process information).

Fundamental elements of memory involve the degree of attention to a stimulus and the subsequent encoding of information for storage and retrieval. Two ERP components that are useful to measure these aspects of memory are P300a and P300b[7]. The P300b component has been exceptionally well-studied with regard to memory loss disorders such as Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD). Longer

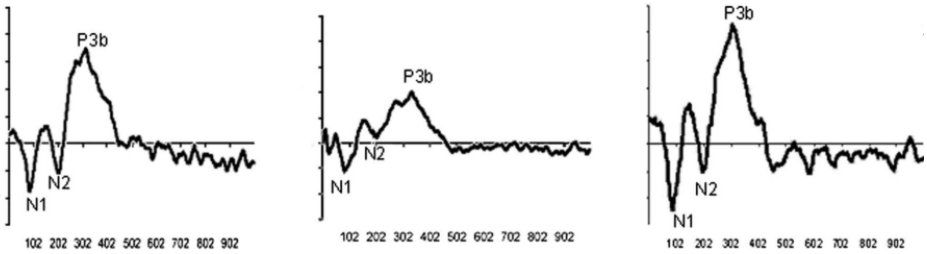

Figure 2. Grand average ERPs for patients with MCI who progressed in dementia symptoms and, patients with MCI who did not progress, and control subjects. MCI Progressors show elongated P300b latency and reduced P300b amplitude[9].

P300b latency measures and low amplitudes have been observed in subjects with mild AD compared to age-matched controls[8]. P300b latency and amplitude have also been shown to predict the progression of mild cognitive impairment[9] (Figure 2). Additionally, P300b metrics demonstrate superior sensitivity over conventional assessments such as the MMSE in detecting early pre-clinical memory loss[10].

Peak Alpha Frequency. The alpha frequency band (8 – 12 Hz), is the most dominant EEG frequency found in the brain. The peak frequency within this frequency band, fittingly termed Peak Alpha Frequency (PAF) or posterior dominant rhythm, is largely generated by the thalamus and reflects thalamo-cortical network activity. PAF can therefore be conceptualized as the pacemaker of the brain and is known to be a good measure of information processing capacity[11].

EEG studies have found that PAF rises from childhood to adolescence, and then decreases slowly with age[11]. Regardless of age, individuals with strong working memory abilities have faster PAF compared to inferior memory performers[12]. Abnormally low PAF (< 8 Hz) can be found in patients with cognitive disturbances and dementia[12,13] (Figure 3) and slowed PAF is correlated with loss of hippocampal volume in many posterior regions of interest in patients with MCI[14]. The PAF electrophysiology biomarker can therefore be used to help identify patients with pre-clinical dementia and monitor patients' overall cognitive capacity over time.

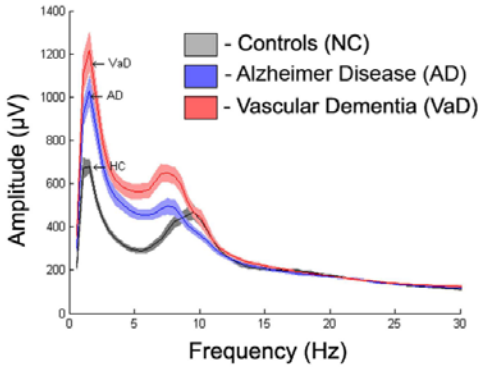

Figure X. EEG spectral features discriminate between AD, VaD, and controls. Demented patients show hallmark qEEG slowing[17] and reduced PAF[12].

Quantitative EEG. Quantitative EEG (qEEG) moves beyond the conventional visual inspection of EEG to perform a strictly objective analysis of brain function. Patients' digital EEG data are statistically analyzed and can be compared to normative database reference values to provide insight to differential diagnosis and treatment effects[15,16]. Distinct differences in resting-state qEEG profiles exist between patients with dementia diagnoses and age-matched controls. Research has shown that some patients with dementia present with slowing of the alpha rhythm and a general decrease in beta power (Figure 3). This qEEG pattern and others may be especially useful in distinguishing dementia from pseudo-dementia. Moreover, qEEG brain maps can provide information relevant to discriminate between specific dementia diagnoses, such as AD and vascular dementia[17]. The sensitivity of qEEG therefore allows for a useful assessment measure when considering memory impairment etiology.

Conclusions. There has been a clear need for objective memory-related measures that aid physicians in developing timely and accurate diagnoses. The eVox® system is a convenient, accessible, and affordable medical device that delivers objective memory loss biomarkers to support doctors in recognizing pre-clinical dementia conditions, identifying the root cause of memory loss, and performing a differential diagnosis.

References

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